

### *REMARKS*

The amendments set out above and the following remarks are believed responsive to the points raised by the Office Action dated November 3, 2004. In view of the amendments set out above and the following remarks, reconsideration is respectfully requested.

#### *The Pending Claims*

Claims 2-5, 7, 8, and 11 have been canceled, and claims 1, 6, 9, 10, and 12 remain pending. Claims 13-15 are added by this amendment.

Several changes have been made in the specification to improve its form. These changes are essentially editorial in nature and do not constitute the addition of new matter.

Claims 1 and 6 have been amended, and claims 13-15 have been added, to describe the invention more clearly. No new matter has been added, the basis for the amended claim language may be found within the original specification, claims and drawings.

Claim 1 is supported at, for example, page 11, line 15, page 19, lines 12-14, page 21, line 10, and page 22, line 6. Claims 6 and 14 are supported at, for example, Examples 1-4. Claim 13 is supported at, for example, Example 1. Claim 15 is supported at, for example, page 22, lines 6-8. Entry of the above is respectfully requested.

#### *The Office Action*

For convenience, the following remarks will address the rejections in the same order they were raised in the Office Action.

#### *Rejections under 35 U.S.C. §112 second paragraph*

Claims 1-12 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. According to the Office Action, with respect to claim 1, it was unclear what was prepared as the final product, and it was unclear what bubbling was intended to convey. With respect to claims 3 and 4, the Office Action alleged the claims recited temperatures well below freezing, and with respect to claim 5, the Office Action alleged the expression "while flowing or after flowing the condensed solution" was unclear.

The claims have been amended to improve the form of the claims and more distinctly claim the subject matter which Applicants regard as their invention.

For example, claim 1 has been amended to more distinctly indicate that the claimed method for producing a liposome preparation by vacuum drying comprises preparing a liposome condensed solution by removing solvent from a liposome solution, the liposome solution

comprising tacrolimus or its hydrate, a liposome-forming lipid, at least one stabilizer and solvent; and subjecting the liposome condensed solution to vacuum drying wherein under vacuum condition the temperature of the condensed solution is lowered to the range from -30°C to -40°C and then the temperature of the condensed solution is raised to 30°C to 50°C to bubble the condensed solution, in which vacuum drying is carried out without freezing while bubbling the condensed solution or after bubbling the condensed solution. It is respectfully submitted that one of ordinary skill in the art reading the application (including Examples 1-4; *see also*, the list of the properties of the liposome preparation prepared in the Examples in Table 1) would understand what is being claimed.

With respect to bubbling, as described in the application (*see, for example*, page 18, line 25, through page 19, line 23, as well as Examples 1-4), a bubble can be generated by thermal change, and thus does not require a gas.

With respect to vacuum drying without drying, the liposome condensed solution includes a stabilizer (e.g., maltose), and thus, does not freeze at the while being vacuum dried at -30°C to -40°C. Accordingly, while the rejection is moot as applied to claims 3 and 4 as they have been canceled, the rejection should not be applied to newly submitted claim 13.

Claim 5 has been canceled, thus rendering the rejection moot.

Thus, it is respectfully submitted that with these remarks and amendments to the claims, the rejections under 35 U.S.C. §112 have now been overcome and should be withdrawn.

*Rejections under 35 U.S.C. §§102 and 103*

Claims 1-3, 5, 6, 9, 10 and 12 were rejected under 35 U.S.C. §102 as anticipated by International Publication No. WO 92/22298 (hereinafter referred to as "WO '298").

Claims 1, 5, 6, 9, and 12 were rejected under 35 U.S.C. §102 as anticipated by International Publication No. WO 86/01103 (hereinafter referred to as "WO '103") or Japanese Publication No. JP 06 315623 (hereinafter referred to as "JP '623").

Claims 8 and 11 were rejected under 35 U.S.C. §103(a) as being unpatentable over WO '298, or WO '103 or JP '623, further in view of European Published Application No. EP 658,344 (hereinafter referred to as "EP '344").

Each of these rejections is separately and respectfully traversed.

With respect to the rejections under 35 U.S.C. §102, there is no disclosure in any of WO '298, WO '103, or JP '623 of tacrolimus or its hydrate, and there is no disclosure in any of these documents of bubbling, particularly "wherein under vacuum conditions the temperature of the

condensed solution is lowered to the range from -30°C to -40°C, and then the temperature of the condensed solution is raised to 30°C to 50°C to bubble the condensed solution” as is presently claimed in independent claim 1. With respect to newly added dependent claim 13, there is no disclosure in these documents of raising the temperature of the condensed solution to 40°C from -40°C.

Moreover, none of these documents suggests the effect of the claimed process, i.e., the superior permeability after redispersion wherein precipitates are not formed after mixing with blood plasma (*see, for example*, Examples 1-4, particularly, Table 1, and page 26, lines 17-24, as well as page 28, lines 18-23).

Accordingly, WO ‘298, WO ‘103, and JP ‘623, whether taken alone or together, fail to anticipate or suggest the process for producing a liposome preparation claimed in claim 1, and thus, the rejection cannot be maintained.

The process of the present invention is patentably distinct from that of WO ‘298, WO ‘103, and JP ‘623 for the reasons set forth above. The fact that EP ‘344 may teach FK 506 is of no import. EP ‘344 simply does not cure the deficiencies of WO ‘298, WO ‘103, and JP ‘623, and therefore, the combination also fails to render the present invention obvious.

Since the independent claims are allowable for the reasons set forth above, the dependent claims are allowable as they depend from the novel and non-obvious independent claims.

For the reasons set forth above, reconsideration of the rejections is respectfully requested.

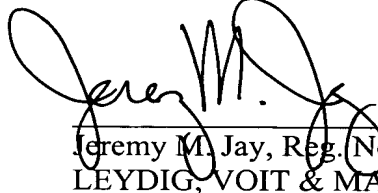
### *Conclusion*

In view of the amendment and remarks recited herein, the application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue.

In re Appln. of OHTOMO et al.  
Application No. 10/089,084

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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